

**Notice of Allowability**

Application No.

10/087,188

Examiner

David A. Saunders, PhD

Applicant(s)

ROSE ET AL.

Art Unit

1644

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to AMEND OF 5/20/05.
2. ☒ The allowed claim(s) is/are 1-13,15-17,19-21,23-54,57-61,65,68-72 and 74.
3. ☒ The drawings filed on 28 February 2002 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of the:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.  
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached  
1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.  
(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |   |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)  | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)           |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                | 6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____ |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),<br>Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment                   |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material          | 8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance             |
|   | 9. <input type="checkbox"/> Other _____   |

Art Unit: 1644

The after FINAL amendment filed on 5/20/05 has been entered.

An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted on 6/10/05, Joseph Snyder requested an extension of time for ONE MONTH(S) and authorized the Director to charge Deposit Account No. 20-1430 the required fee of \$ 60.00 for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Claim 72, as presented in the after FINAL amendment, has been amended as follows:

-- 72. (Currently amended) A method of diagnosing the presence or severity of liver fibrosis in an individual, comprising the steps of:

(a) comparing a level of a first fibrotic marker  $\alpha$ 2-MG in said individual to a cut-off value X1 to determine whether said individual is positive for  $\alpha$ 2-MG, wherein said individual is positive for  $\alpha$ 2-MG when said level of  $\alpha$ 2-MG is above X1;

(b) comparing a level of a second fibrotic marker HA in said individual to a cut-off value Y1 to determine whether said individual is positive for HA, wherein said individual is positive for HA when said level of HA is above Y1;

(c) comparing a level of a third fibrotic marker TIMP-1 in said individual to a cut-off value Z1 to determine whether said individual is positive for TIMP-1, wherein said individual is positive for TIMP-1 when said level of TIMP-1 is above Z1,

Art Unit: 1644

wherein ~~said~~ any individual positive for  $\alpha$ 2-MG, HA, and TIMP-1 as compared to X1, Y1, and Z1, respectively, is further evaluated for positivity for  $\alpha$ 2-MG, HA, and TIMP-1 using a second set of cut-off values X2, Y2, and Z2 comprising:

(d) comparing the level of  $\alpha$ 2-MG in said individual to X2, wherein said individual is positive for  $\alpha$ 2-MG when said level of  $\alpha$ 2-MG is above X2;

(e) comparing the level of HA in said individual to Y2, wherein said individual is positive for HA when said level of HA is above Y2;

(f) comparing the level of TIMP-1 in said individual to Z2, wherein said individual is positive for TIMP-1 when said level of TIMP-1 is above Z2; and

(g) diagnosing the presence or severity of liver fibrosis in said individual based on positivity or negativity for  $\alpha$ 2-MG, HA, and TIMP-1, wherein said cut-off values X2, Y2, and Z2 are greater than or equal to X1, Y1, and Z1, respectively, ~~and wherein said cut-off values X1, Y1, Z1, X2, Y2, and Z2 are independently selected to achieve an optimized clinical parameter selected from the group consisting of sensitivity, specificity, negative predictive value, positive predictive value, and accuracy~~

wherein said individual is diagnosed as having liver fibrosis when said individual is positive for  $\alpha$ 2-MG, HA, and TIMP-1 as compared to X2, Y2, and Z2, respectively, and

wherein said individual is diagnosed as having an indeterminate status when said individual is negative for  $\alpha$ 2-MG, HA, or TIMP-1 as compared to X2, Y2, and Z2, respectively. --

The above amendment is supported by the disclosure, most particularly at page 102, line 10-page 103, line 3.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

Art Unit: 1644

supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 6/10/05 DAS



DAVID SAUNDERS  
PRIMARY EXAMINER  
ART UNIT ~~102~~ 1644